What is Claimed is:

1. An isolated and purified growth factor comprising neurturin.

2. The isolated and purified growth factor of claim 1 wherein the amino acid sequence contains a sequence as set forth in SEQ ID NO:31.

3. The isolated and purified growth factor of claim 1 wherein the amino acid sequence contains a mature human neurturin as set forth in SEQ ID NO:1.

4. The isolated and purified growth factor of claim 3 in a pharmaceutically acceptable carrier.

5. The isolated and purified growth factor of claim 1 produced by recombinant DNA technology.

6. The isolated and purified growth factor of claim 1 comprising a monomeric polypeptide.

7. The isolated and purified growth factor of claim 6 comprising a homodimeric polypeptide.

8. The isolated and purified protein of claim 7 which has an apparent molecular weight of approximately 10-15 kD as determined from SDS-PAGE under reducing conditions.

9. An isolated and purified growth factor comprising a protein having the following characteristics:

(a) an apparent molecular weight of approximately 20-30 kD as determined by SDS-PAGE under non-reducing conditions;

(b) an $EC_{50}$ in a superior cervical ganglion survival assay less than about 10 ng/ml;

(c) the protein can be identified in or obtained from cells obtained from ovary cells; and

(d) the protein binds to a heparin agarose matrix in a pH 7.4 buffer containing 0.5 M NaCl, but not in a pH 7.4 buffer containing 1.0 M NaCl.

10. The isolated and purified growth factor of claim 9 wherein the factor is comprised of an amino acid sequence of mature human growth factor as set forth in SEQ ID NO:1.

11. The isolated and purified growth factor of claim 10 in a pharmaceutically acceptable carrier.

12. An isolated and purified protein comprising pre-pro neurturin.

13. The isolated and purified protein of claim 12 wherein the pre-pro neurturin is human pre-pro neurturin as set forth in SEQ ID NO:7 or a derivative thereof.

14. An isolated and purified protein comprising a signal peptide which is a pre- region of neurturin or a fragment thereof.

15. The isolated and purified protein of claim 14 wherein the pre- region is a human pre- region as set forth in SEQ ID NO:15 or a fragment thereof.

16. An isolated and purified protein comprising a peptide which is a pro-region of neurturin or a fragment thereof.

17. The isolated and purified protein of claim 16 wherein the pro- region is a human pro- region as set forth in SEQ ID NO: 19 or a fragment thereof.

18. An isolated and purified growth factor that is a neurturin family member comprising an amino acid sequence having between about 30% and about 85% sequence identity with neurturin and between about 30% and about 85% sequence identity with GDNF.

19. The isolated and purified growth factor of claim 18 wherein said factor is comprised of a conserved region amino acid sequence having at least 62.5 percent sequence identity with SEQ ID NO:33 or at least 40 percent sequence identity with SEQ ID NO:34 or at least 40 percent sequence identity with SEQ ID NO:35.

20. The isolated and purified growth factor of claim 18 wherein said factor is encoded by a nucleotide sequence identified and/or obtained by the polymerase chain reaction method utilizing a primer containing a nucleotide sequence selected from the group consisting of SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, and SEQ ID NO:48.

21. The isolated and purified growth factor of claim 18 wherein said factor is identified and/or obtained by reacting said factor with an antibody capable of reacting with a polypeptide containing an amino acid sequence encoded by a polynucleotide selected from the group consisting of SEQ ID NO:33, SEQ ID NO:34 and SEQ ID NO:35.

22. An isolated and purified nucleic acid sequence comprising a nucleotide sequence encoding neurturin.

23. The isolated and purified nucleic acid sequence of claim 22 comprising a nucleotide sequence encoding a human neurturin amino acid sequence as set forth in SEQ ID NO:1.

24. The isolated and purified nucleic acid sequence of claim 22 comprising a human neurturin nucleotide sequence as set forth in SEQ ID NO:9.

25. An isolated and purified nucleic acid sequence comprising a nucleotide sequence encoding pre-pro neurturin.

26. The isolated and purified nucleic acid sequence of claim 25 comprising a nucleotide sequence encoding a human pre-pro neurturin amino acid sequence as set forth in SEQ ID NO:7.

27. The isolated and purified nucleic acid sequence of claim 26 comprising a human pre-pro neurturin nucleotide sequence as set forth in SEQ ID NO:11.

28. An isolated and purified nucleic acid sequence comprising a nucleotide sequence encoding a pre- region of a pre-pro neurturin or a fragment of said pre- region.

29. The isolated and purified nucleic acid sequence of claim 28 comprising a nucleotide sequence encoding a human pre- region amino acid sequence as set forth in SEQ ID NO:15 or a fragment thereof.

30. The isolated and purified nucleic acid sequence of claim 29 comprising a human pre- region nucleotide sequence as set forth in SEQ ID NO:17.

31. An isolated and purified nucleic acid sequence comprising a nucleotide sequence encoding a pro- region of neurturin.

32. The isolated and purified nucleic acid sequence of claim 31 comprising a nucleotide sequence encoding a human neurturin pro- region amino acid sequence as set forth in SEQ ID NO:19.

33. The isolated and purified nucleic acid sequence of claim 32 comprising a human neurturin pro-region nucleotide sequence as set forth in SEQ ID NO:20.

34. An isolated and purified nucleic acid sequence which hybridizes to a nucleotide sequence complementary to a nucleic acid sequence selected from the group consisting of:

(a) a nucleic acid sequence which encodes an amino acid sequence for pre-pro human growth factor as set forth in SEQ ID NO:7;

(b) a nucleic acid sequence which encodes an amino acid sequence for mature human growth factor as set forth in SEQ ID NO:1;

(c) a nucleic acid sequence which encodes an amino acid sequence which cross-reacts with mature human growth factor as set forth in SEQ ID NO:1.

35. A vector comprising a recombinant DNA molecule comprising expression regulatory elements operably linked

to a nucleic acid sequence encoding a growth factor as defined in claim 1.

36. The vector of claim 35 wherein said vector is pCMV-NTN-3-1.

37. The vector of claim 35 wherein said vector is pET-NTN.

38. A host cell transformed with the vector of claim 35.

39. The host cell of claim 38 wherein said host cell is a mammalian cell.

40. The host cell of claim 39 wherein said host cell is a DG44 cell or derivative thereof.

41. The host cell of claim 40 wherein said host cell is DG44CHO5-3(G418)(pCMV-NTN-3-1).

42. The host cell of claim 40 wherein said host cell is DG44CHO5-3(50nMMTX)(pCMV-NTN-3-1).

43. The host cell of claim 38 wherein the host cell is a bacterial cell.

44. The host cell of claim 38 wherein said host cell is a baculovirus expression system.

45. A recombinant DNA method comprising:

(a) subcloning a DNA sequence encoding a growth factor as defined in claim 1 into an expression vector which comprises regulatory elements needed to express the DNA sequence;

(b) transforming a host cell with said expression vector;

(c) growing the host cell in a host cell culture; and

(d) harvesting the growth factor and/or the DNA sequence from the host cell culture.

46. The method according to claim 45 wherein the host cell is as a mammalian cell, a bacterial cell or a baculovirus expression system.

47. Isolated and purified antibodies which are capable of reacting with a growth factor as defined in claim 1 or an epitope thereof.

48. A method for preventing or treating cellular degeneration or insufficiency comprising administering to a patient a therapeutically effective amount of a growth factor as defined in claim 1.

49. The method of claim 48 wherein the growth factor comprises mature human neurturin as set forth in SEQ ID NO:1.

50. The method of claim 49 wherein the cellular degeneration is comprised of neuronal degeneration resulting from a condition selected from the group consisting of peripheral neuropathy, amyotrophic lateral sclerosis, Alzheimer's disease, Parkinson's disease, Huntington's disease, Ischemic stroke, acute brain injury, acute spinal chord injury, nervous system tumors, multiple sclerosis, and infection.

51. The method of claim 49 wherein the cellular degeneration or insufficiency is comprised of hematopoietic cell degeneration or insufficiency selected from the from the group consisting of eosinopenia, basopenia, lymphopenia, monocytopenia, neutropenia, anemias, thrombocytopenia, and stem-cell insufficiencies therefor.

52. A method for preventing or treating cellular degeneration or insufficiency comprising administering to a patient a composition comprising a DNA sequence as defined in claim 22.

53. The method of claim 52 wherein the cellular degeneration is comprised of neuronal degeneration.

54. The method of claim 53 wherein the neuronal degeneration results from a condition selected from the group consisting of peripheral neuropathy, amyotrophic lateral sclerosis, Alzheimer's disease, Parkinson's

disease, Huntington's disease, Ischemic stroke, acute brain injury, acute spinal chord injury, nervous system tumors, multiple sclerosis, and infection.

55. The method of claim 52 wherein the cellular degeneration or insufficiency is comprised of hematopoietic cell degeneration or insufficiency.

56. The method of claim 55 wherein the hematopoietic cell degeneration or insufficiency results from a condition selected from the group consisting of eosinopenia, basopenia, lymphopenia, monocytopenia, neutropenia, anemias, thrombocytopenia, and stem-cell insufficiencies therefor.

57. The method of claim 52 wherein the method comprises implanting cells that express a growth factor as defined in claim 1 into a patient.

58. The method of claim 57 wherein the growth factor comprises mature human neurturin as set forth in SEQ ID NO:1.

59. The method of claim 58 wherein the cellular degeneration is comprised of neuronal degeneration resulting from a condition selected from the group consisting of peripheral neuropathy, amyotrophic lateral sclerosis, Alzheimer's disease, Parkinson's disease, Huntington's disease, Ischemic stroke, acute brain injury, acute spinal chord injury, nervous system tumors, multiple sclerosis, and infection.

60. The method of claim 58 wherein the cellular degeneration or insufficiency is comprised of hematopoietic cell degeneration or insufficiency selected from the group consisting of eosinopenia, basopenia, lymphopenia, monocytopenia, neutropenia, anemias, thrombocytopenia, and stem-cell insufficiencies therefor.

61. A method for detecting the presence of a growth factor in a sample from a patient comprising reacting purified antibodies according to claim 51 with a

growth factor present in the sample and detecting a binding of the antibodies with the growth factor.

62. A kit for detecting the presence of a growth factor in a sample from a patient comprising antibodies according to claim 51 wherein the antibodies are capable of detectably reacting with a growth factor as defined in claim 1, packaged in a container.

63. A method for detecting the presence of a growth factor in a sample from a patient comprising detecting and/or quantitating the presence of mRNA encoding an amino acid sequence as set forth in SEQ ID NO:1 or a derivative thereof in the sample.

64. The method according to claim 63 wherein the detecting and/or quantitating step is comprised of the steps of:

(a) providing a polynucleotide containing a nucleic acid sequence that encodes an amino acid sequence as set forth in SEQ ID NO:1 or a derivative thereof or a fragment thereof;

(b) incubating the polynucleotide with the sample under conditions in which the polynucleotide can hybridize with mRNA from the sample; and

(c) detecting the existence of a DNA-RNA hybridization complex.

65. A kit for detecting the presence of a growth factor in a sample from a patient comprising a polynucleotide containing a nucleic acid sequence that encodes an amino acid sequence as set forth in SEQ ID NO:1 or a derivative thereof or a fragment thereof, packaged in a container.

66. The method according to claim 63 wherein the detecting and/or quantitating step is comprised of the steps of:

(a) producing a cDNA from mRNA using a reverse transcription method in a sample obtained from a patient,

(b) providing two oligonucleotides which are primers for a polymerase chain reaction method and which flank a target DNA sequence which lies within a cDNA encoding an amino acid sequence as set forth in SEQ ID NO:1,

(c) amplifying the target DNA sequence by the polymerase chain reaction method, and

(d) detecting the presence of the amplified target DNA sequence.

67. A kit for detection of the presence a growth factor in a sample from a patient comprising two oligonucleotides which are primers for the polymerase chain reaction method and which flank a target DNA sequence which lies within a cDNA sequence encoding an amino acid sequence as set forth in SEQ ID NO:1, packaged in a container.

68. A method for detecting neurturin gene alterations comprising detecting the presence of an intact neurturin gene in a cell wherein absence of the intact gene indicates the presence of gene alterations.

69. The method according to claim 68 wherein the detecting step further comprises the steps of:

(a) providing two oligonucleotides which are primers for the polymerase chain reaction method and which are capable of amplifying a target DNA sequence that lies within a neurturin gene,

(b) amplifying the target DNA sequence, and

(c) detecting the presence or absence of an amplified DNA sequence from an intact neurturin gene.

70. The method according to claim 68 wherein the detecting step comprises directly sequencing the amplified target DNA sequence.

71. The method according to claim 69 wherein the target DNA sequence is comprised of a nucleic acid

sequence that flanks or lies within an exon of pre-pro neurturin.

72. A kit for detecting neurturin gene alterations in a cell comprising two oligonucleotides which are primers for the polymerase chain reaction method and which are capable of amplifying a DNA sequence which lies within a neurturin gene, packaged in a container.

73. The method according to claim 67 wherein the detecting step is comprised of the steps of:

(a) providing an oligonucleotide that is capable of hybridizing with an intact neurturin gene,

(b) incubating the oligonucleotide with the sample under conditions in which the oligonucleotide can hybridize with an intact neurturin gene, and

(c) detecting the presence or absence of a DNA-DNA hybridization complex.

74. The method according to claim 73 wherein the oligonucleotide contains an exon of pre-pro neurturin or a fragment thereof.

75. A kit for detecting alterations in a neurturin gene comprising an oligonucleotide which is capable of hybridizing with an intact neurturin gene packaged in a container.

76. The kit according to claim 75 wherein the oligonucleotide contains an exon of pre-pro neurturin or a fragment thereof.

77. A method for promoting the growth and/or differentiation of a cell in a culture medium comprising administering to the cell a growth factor as defined in claim 1.

78. The method according to claim 77 wherein the cell is hematopoietic cell or stem cell thereof.

79. The method according to claim 77 wherein the cell is a neuronal cell or stem cell thereof.

80. A method for treating tumor cells in a patient comprising administrating an effective amount of a growth factor as defined in claim 1.

81. The method according to claim 81 wherein the tumor cells neuroblastoma cells.

82. A method for treating tumor cells in a patient comprising administering a composition comprising a DNA sequence as defined in claim 22.

83. The method according to claim 82 wherein the tumor cells neuroblastoma cells.

84. An isolated and purified neurturin antisense polynucleotide comprising a sequence or derivative thereof wherein the sequence or derivative thereof is complementary to and capable of hybridizing with a naturally-occurring DNA or mRNA polynucleotide sequence encoding neurturin to prevent transcription and/or translation of an encoded neurturin polypeptide.

85. The isolated and purified neurturin antisense polynucleotide of claim 84 wherein said polynucleotide is comprised of from about 15 to about 30 consecutive nucleotides.

86. The isolated and purified neurturin antisense polynucleotide of claim 85 wherein the polynucleotide is comprised of at least one linkage selected from the group consisting of phosphotriester, phosphorothioate, methylphosphonate, phosphoramidate, phosphorodithioate formacetal, dithioate, morpholino and peptide nucleic acid analogue.

87. A method for treating a disease condition mediated by the expression of neurturin in a cell comprising administering an inhibitory effective amount of an isolated and purified antisense polynucleotide or derivative thereof wherein the polynucleotide or derivative thereof is complementary to and capable of hybridizing with a naturally-occurring DNA or mRNA

polynucleotide sequence encoding neurturin to prevent transcription and/or translation of an encoded neurturin polypeptide.

88. The method according to claim 87 wherein said polynucleotide is comprised of from about 15 to about 30 consecutive nucleotides.

89. The method according to 88 wherein the polynucleotide is comprised of at least one linkage selected from the group consisting of phosphotriester, phosphorothioate, methylphosphonate, phosphoramidate, phosphorodithioate formacetal, dithioate, morpholino and peptide nucleic acid analogue.

90. The method according to claim 87 wherein the disease condition is obesity.

91. A hybrid polypeptide comprising a first sequence that is substantially identical to a portion of neurturin and a second sequence that is substantially identical to a portion of a TGF-β superfamily member other than neurturin.

92. The hybrid polypeptide according to claim 91 wherein the first sequence is substantially identical to SEQ ID NO:109 and the second sequence is substantially identical to a sequence selected from the group consisting of SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, and SEQ ID NO:132.

93. The hybrid polypeptide according to claim 91 wherein the first sequence is substantially identical to SEQ ID NO:133 and the second sequence is substantially identical to a sequence selected from the group consisting of SEQ ID NO: 86, SEQ ID NO:87, SEQ ID NO:88,

SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, and SEQ ID NO:108.

94. A DNA molecule encoding the hybrid polypeptide according to claim 91.

95. An expression vector comprising the DNA molecule of claim 94.

96. A host cell comprising the DNA molecule of claim 94.

97. A pan-growth factor comprising an active domain of neurturin and an active domain of at least one growth factor other than neurturin.

98. The pan-growth factor according to claim 97 comprising human neurturin and at least one growth factor other than neurturin selected from the group consisting of NGF, BDNF, NT-3, NT-4/5, a TGF-β superfamily member, vascular endothelial growth factor, and a member of the CNTF/LIF family.

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